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Predictors Of A Differential Neural Response To Infant Cues In Substance Using And Non-Using Mothers

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Abstract

PREDICTORS OF A DIFFERENTIAL NEURAL RESPONSE TO INFANT CUES IN SUBSTANCE USING AND NON-USING MOTHERS. *Marjorie-Anne R. Guerra, Helena J.V. Rutherford, Linda C. Mayes. Child Study Center, Yale University School of Medicine, New Haven, CT.*

Substance use during pregnancy and the postpartum period impacts not only the substance using mother, but also her infant by affecting the mother's ability to provide care during this critical time period. Current research demonstrates the neural circuitry of the reward and stress systems important in parenting overlaps with the circuitry dysregulated in addictive processes, which may compromise a mother's ability to respond appropriately to infant cues. In the initial study, parental sensitivity to infant cues was examined in substance using and non-using mothers. Participants viewed images of infant faces while simultaneous electroencephalography (EEG) recorded their neural responses. EEG data showed that the latency of the face-specific N170 event-related potential (ERP) peaked later in substance using mothers relative to non-using mothers, but no difference was observed in the earlier P1 ERP component, a marker of general visual processing. The present study investigated predictors of this differential neural response to infant faces by analyzing self-reported measures of behavioral motivation systems (Behavioral Inhibition System/Behavioral Activation System Scale), impulsivity (Barratt Impulsiveness Scale-11), and parenting stress (Parenting Stress Index-Short Form). It was hypothesized that compared to non-using mothers, substance using mothers would score higher in measures of the behavioral activation motivation system, impulsivity, and parental stress, and would score lower in

measures of the behavioral inhibition motivation system, and that these scores would correlate with a later latency of the N170. Results showed that substance using mothers scored higher in measures of impulsivity, behavioral activation motivation system sensitivity, and one measure of parental stress. Results showed that a later N170 latency correlated with a higher fun-seeking score of the behavioral activation motivation system (Pearson's $r = .274$, $p<.05$), a higher score of the cognitive complexity factor of impulsivity (Pearson's $r = .260$, $p=.06$), and a higher score of parental distress (Pearson's $r = .253$, $p=.09$). Taken together, these results suggest that early visual processing of infant faces may be compromised in mothers with higher BAS fun-seeking sensitivity, higher impulsivity related to cognitive complexity, and higher parental distress. Given that these traits are more likely to be found in substance users, these results lend further suggestive evidence to the hypothesis that parenting can be compromised in addictive states due to an impairment in reward sensitivity and stress reactivity to infant cues.

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Introduction

The transition to motherhood, including the development of sensitivity to infant cues and maternal behaviors, is crucial for both the immediate care of the infant and the long-term development of the child, including cognitive development (1), stress reactivity (2), and future maternal care (2, 3). This transition involves significant psychological and neurobiological changes. Specifically, adaptations in the neural circuitry mediating reward and stress appear to affect a mother's ability to respond appropriately to infant cues (4). These pathways overlap with the neural pathways that are dysregulated in the addicted state (5). The current study was part of a larger study by Rutherford et al. (6), in which a differential brain response as measured by electroencephalography (EEG) was found in response to visual infant cues in substance using mothers relative to non-using mothers. The purpose of this thesis was to investigate whether this differential sensitivity to visual infant cues was associated with differences in measures of behavioral motivation, impulsivity and parental stress.

The rewarding experience of motherhood

Although parenthood is a demanding role, it is also a potentially intensely satisfying experience as evidenced by activation of key reward pathways in the brain. The neural circuitry underlying the reward system includes the pathways connecting the ventral tegmental area (VTA) of the midbrain with the nucleus accumbens (NAc) and prefrontal cortex (PFC), with dopamine serving as the major

neurotransmitter mediating these pathways (5). In preclinical models, pup suckling has been found to activate these dopaminergic reward pathways in dams (7). Similarly, fMRI studies of first-time human mothers showed activation of the VTA, striatum, and frontal lobe when viewing images of their own infant's faces smiling but not crying (8). The reward associated with infant cues and maternal behavior may in fact serve an important adaptive function, as it motivates initiation and maintenance of maternal behaviors.

As a result, a mother must be able to appropriately gauge the rewarding value of a stimulus, a cognitive function that is mediated by the VTA (5). In rodents, pharmacological inactivation of the VTA results in deficits in maternal behaviors (9). The VTA is also an important source of dopamine, with projections to the NAc and PFC. In lactating rats, pup licking and grooming is associated with significantly increased dopamine in the NAc (10). Interestingly, the increased signal was noted prior to the onset of the behavior and the concentration of dopamine correlated directly with duration of the behavior, suggesting the importance of the dopaminergic signal in mediating the motivation of the behavior.

The PFC serves a variety of cognitive functions, such as motivation, self-control, decision-making, goal-oriented activity, working memory, and attention shifting (10, 11), and thus can influence maternal behavior on a number of levels. In rats, disruptions to the PFC cause deficits in some maternal behaviors and a disorganization of the pattern of maternal behavior (12), which may be explained in part by impairments in motivation and working memory, respectively. In functional

magnetic resonance imaging studies of human mothers, the orbitofrontal cortex (OFC) was activated bilaterally when viewing pictures of infants, with activation correlating with pleasant mood scores (13). This suggests the role of the OFC in mediating sensitivity to infant cues, which is further influenced by maternal characteristics such as mood.

Importantly, the medial PFC and OFC have both been shown to be important mediators of impulsivity (14), with dopamine serving as a major neurotransmitter (15). A recent preclinical study suggests that impulsivity indeed affects maternal behavior, as rats that demonstrated higher levels of impulsivity on efficiency tasks spent less time on maternal behaviors (16). Impulsivity has been defined as "predisposition toward rapid, unplanned reactions to internal and external stimuli without regard for the negative consequences of these reactions to themselves or others" (17). Accordingly, impulsive mothers may act towards a non-infant stimulus at the expense of the care of her infant because they view the non-infant stimulus as more rewarding than their own infant.

In summary, these studies indicate the importance of the reward neural pathways in motivating maternal behavior and the potential for individual differences in mediating these pathways.

Effects of substance use on the reward neural circuitry of the brain

The use of drugs of abuse continues to be a significant public health issue in the United States. Approximately 15.6% of the population participates in nonmedical or illicit drug use during their lifetime, and of this group, 20.1% will continue on to drug abuse while 18.6% will continue on to drug dependence (18). It is important to note that the present study is based under the framework that substance use reflects an *addictive process* impacting the reward and stress neural systems more generally, leading to the gradual development of habitual drug-seeking behavior.

The acute rewarding effects of all drugs of abuse appear to be mediated by the mesolimbic pathways. In one study using brain dialysis in rats, it was found that opiates, ethanol, nicotine, amphetamine, and cocaine all increased extracellular dopamine concentrations in the septi of the nucleus accumbens (19). Currently, it is thought that the acute rewarding effect of drugs of abuse are mediated in various manners involving the mesolimbic pathways: cocaine, amphetamine, and nicotine through dopamine release in the NAc; opiates through opioid peptide receptor activation in the VTA and NAc; and alcohol through the NAc and amygdala (5). In addition, reinforcement of drug-seeking behavior appears to be mediated by the mesolimbic system in cocaine and amphetamines, though this is not necessarily true in other drugs of abuse such as heroin or ethanol (5).

The PFC is also disrupted in addiction, leading to deficits in important executive functions such as motivation and self-control. In the addicted state, behavior toward non-drug stimuli may be decreased due to impaired salience of

these stimuli. In a study by Goldstein and colleagues (20), the sensitivity to relative monetary value was assessed in cocaine-addicted individuals by presenting them with a gradient of monetary rewards, ranging from $10-$1000. Interestingly, over half of the cocaine-addicted subjects valued all monetary amounts equally, and this response was associated with higher activations in the lateral OFC and frontal gyrus and lower activations in the middle frontal gyrus when compared to the cocaine-addicted participants who did not show this impaired valuation. This finding suggested that addicted individuals have an impaired ability to judge the value of non-drug stimuli, which may be due to impaired reward salience of the stimuli when compared to drugs of abuse. Additionally, the imaging findings suggested that this deficit was associated with a differential activation of the PFC.

Furthermore, the PFC is involved in self-control, which is impaired in addictive processes. Based on neuroimaging studies over the past 10 years, Goldstein and Volkow (11) propose that addiction leads to an impaired ability of higher order cognitive input from the PFC to inhibit maladaptive behavior, leading to unregulated drug-seeking behavior. On a behavioral level, the acute rewarding effect of taking the drug leads to positive reinforcement of drug-seeking behavior, eventually leading to impulsivity to acquire and use the substance (5). Individuals with a history of drug dependence indeed show higher levels of impulsivity based on both behavioral and self-report measures (21).

Addictive processes lead to dysregulation of the reward neural circuitry, as described above, which can then lead to imbalances in behavioral motivation

systems. Two key behavioral motivation systems include the behavioral activation system (BAS) and the behavioral inhibition system (BIS), which were proposed to underlie two dimensions of personality: impulsivity and anxiety, respectively (22). The BAS, also known as the appetitive system, activates behavior that leads to rewarding stimuli, with increased BAS sensitivity believed to underscore impulsivity. In addictive processes, the individual has a higher sensitivity to this motivational system, with the acute rewarding effect of the drug serving as the incentive. This may occur at the expense of the salience of other normally rewarding stimuli, such as infant cues. The behavioral inhibition system (BIS), also known as the aversive motivation system, inhibits behavior that leads to negative outcomes. In addictive processes, the individual has less sensitivity to this motivational system acting solely with drugs in mind and without considering the negative medical and social consequences.

In summary, the above findings suggest that addictive processes lead to a dysregulation of the reward neural circuitry, leading to changes in the behavioral motivation systems now driven primarily by the acute rewarding properties of substance use.

Adaptations of the stress system in motherhood

Although motherhood has rewarding properties, pregnancy and the postpartum can be stressful periods for the mother, with direct and indirect implications for the infant. Gestational stress has been shown to directly affect

stress reactivity and future maternal care of lactating female offspring (23). Additionally, alterations in the stress system can indirectly affect the infant due to impaired maternal care. Prenatal stress has been shown to negatively impact maternal behaviors (24-26), highlighting the importance of maintaining a healthy amount of stress during the peripartum period.

The physiological experience of stress is mediated by the hypothalamic-pituitary-adrenal (HPA) axis. In response to an acute stressor, the parvoventricular nucleus of the hypothalamus secretes corticotropin-releasing factor (CRF) into the hypophyseal blood supply, which acts on the anterior pituitary gland to secrete adrenocorticotropic hormone (ACTH) into the blood supply, eventually reaching the adrenal medulla which systemically releases glucocorticoids, namely corticosterone in rats and cortisol in humans (27). This in turn leads to physiological responses in the cardiovascular, autonomic, metabolic, neural, and immune systems (28). The system is regulated by negative feedback induced by the glucocorticoids acting on the pituitary, hypothalamus, and hippocampus.

Throughout pregnancy and the postpartum period, neuroendocrine and neurobiological adaptations take place leading to a differential sensitivity to stressors in mothers. Pregnancy and lactation are characterized by higher basal glucocorticoid levels, decreased hormonal (specifically, hormones of the HPA axis) and emotional responses to stressors, and an increased sense of calmness (29). Oxytocin plays an important role during the peripartum period in partuition and lactation, and emerging data supports its role in mediating this adaptation in the

stress system (29). Both CRF and oxytocin are secreted by the paraventricular nucleus of the hypothalamus, and oxytocin has been shown to decrease CRF mRNA expression (30). In fact, in preclinical models, oxytocin has been shown to reduce the increase in blood pressure caused by prenatal stress (31).

The modification of the stress system in the transition to parenthood is critical. Infant cues such as cries may provide more stress than an individual would otherwise be capable of handling. Administration of corticosterone during pregnancy and the postpartum results in impaired maternal behaviors in dams, such as reduced time spent on nursing and nesting (32). This finding suggests that hyperactivity of the HPA axis may represent an unmanageable stress load that impairs a mother's ability to care for her infant. At the same time, components of the HPA axis are important in modulating maternal behavior. CRF signaling has been shown to play a role in maternal defense behavior (33), as stressful cues from a foreign intruder activate a behavioral response to protect her pups. This highlights the importance of precise regulation of the stress system, as a mother must appropriately judge the stressfulness of cues in providing care to her infant.

In summary, pregnancy and the postpartum represent a dynamic time for the stress neural pathways, which make it vulnerable to influences of motherhood and, potentially, other external factors.

Effects of substance use on the stress neural circuitry of the brain

The stress system has been implicated in the various stages of drug use and addiction. In preclinical models, acute cocaine administration has been shown to increase plasma ACTH and glucocorticoids, which appears to be mediated by cocaine-induced release of CRH from the hypothalamus (27). In pregnant rats, chronic cocaine administration leads to significantly higher levels of corticosterone (34).

Stress plays several roles in the cyclic process of addiction, having effects on both drug abuse and relapse (35). Koob and Volkow (5) propose that stress serves as negative reinforcement during withdrawal, as the HPA axis is activated during withdrawal from all major drugs of abuse. A study in male rats showed that conditioned place aversion to opiate withdrawal can be reversed by a CRF-1 receptor antagonist (36), suggesting the role of CRF in mediating the effect of acute withdrawal. The role of the stress system has also been implicated in relapse. Psychological stress motivates cravings in cocaine abusers (37), an effect that appears to be mediated CRF acting on extrahypothalamic stress pathways such as the amygdala (5, 38, 39).

It has been proposed that the effects of substance use on stress neural circuitry can lead to a maladaptive stress response that perpetuates regular drug abuse and, importantly, alters sensitivity to stressors (35). Mothers who used cocaine during pregnancy reported more life stress and less sense of control (40), though the relationship between stress and substance use is likely bi-directional. In one study, recently abstinent cocaine-dependent individuals showed a higher

sensitivity to negative emotions and increased physiological markers of stress in response to stressful visual cues when compared to social drinkers (41). This provides some evidence towards an enhanced reactivity to stressful stimuli in substance using individuals, at least in the abstinent phase of addiction.

In summary, the above findings suggest that addictive processes lead to a dysregulation of the stress neural circuitry, leading to a maladaptive stress response with altered reactivity to stressful cues.

Assessing maternal sensitivity to infant faces using electrophysiology: the N170

Because infant faces may serve as important cues for motivating maternal behaviors (8), perception of infant faces is a key cognitive function in parenting. The N170 ERP component has been identified as an early marker of face processing, observed in response to human face stimuli but not in response to faces of animals, human hands, and other inanimate objects (42). Specifically, the N170 reflects structural encoding of faces (43).

The N170 is most prominent over the occipito-temporal regions and is larger on the right hemisphere compared to the left hemisphere (42). It has been correlated with areas implicated in face processing, such as the fusiform gyrus and right medial, superior, and inferior temporal gyri (44). Using evidence from neuroimaging studies, a current model suggests that face processing is not solely limited to the fusiform gyrus, and may in fact represent an interaction between the

fusiform gyrus and the amygdala, a key brain region in mediating stress (45). The authors suggest this pathway as the mechanism through which face processing is enhanced by emotional expressions. The N170 has been found to be influenced by top-down factors, such as visual priming (46), although whether it is modulated by emotion is still under debate (6). A recent magnetoencephalography (MEG) study in adults suggests the role of key reward brain regions in generation of the N170 (47). The results show activation of the medial OFC specific to infant faces at around 130 ms. Given its time frame, this MEG activation may be analogous to the N170 ERP component, and may suggest the role of the OFC in generation of the N170.

Face processing is an important element of social interactions, and accumulating evidence supports the notion that the N170 may be influenced by social factors. For example, the N170 has been shown to differentiate individuals with autistic spectrum disorder from those with normal social development (48) and extroverted individuals from introverted individuals (49). Given the potentially intense social interaction between mother and infant, recent studies have started to examine the N170 of mothers in response to infant faces. Of note, these few studies have primarily looked at its effect on N170 amplitude, not latency.

A recent study suggests that the N170 may in fact be modulated by bond formation (50). In this study, it was found that when viewing images of unfamiliar infant faces, the N170 amplitude was enhanced in new parents and new romantic partners relative to romantically unattached singles, suggesting that the transition to parenthood strengthens the neural circuitry involved in processing infant cues

that motivate parental behaviors. This is particularly relevant to substance using mothers, as parental substance use has been shown to negatively impact the parent-child attachment relationship (51).

In a sample of mothers, differences in the N170 were observed between those who were neglectful and those who were non-neglectful (52). Specifically, while viewing images of infants crying, laughing, or with a neutral expression, non-neglectful mothers had the most enhanced N170 amplitude in response to the cry images when compared to the laughter or neutral images. This differentiation was not observed in neglectful mothers. The authors of this study interpret these results to suggest that neglectful mothers may not find the same reward salience in visual infant cues as non-neglectful mothers, and this may ultimately underlie the impaired interaction between neglectful mothers and their children.

In summary, these findings suggest that the N170 generated in response to infant faces may be influenced by individual differences in sensitivity to infant cues.

Compromised parenting in addictive processes

Maternal substance use can have detrimental, if not devastating consequences for both the mother and her infant. It has long been recognized that maternal substance abuse increases the risk of impaired parenting skills (53), and in fact, it has been associated with increased rates of child neglect (54) and child abuse (55). Interactions with infants are also impaired. In one study, cocaine-using

mothers were found to be less responsive to and less interactive with their infants (56). Rats exposed to both nicotine and ethanol during pregnancy were found to have similar impaired interactions with their pups (57). Given the effects of substance use on the reward and stress neural circuitry, parenting may be compromised in addictive processes due to a decreased reward sensitivity and enhanced stress reactivity to infant cues, leading to a deficit in maternal behaviors that are required for the proper care and development of the infant.

Preclinical studies support the idea that substance use may directly affect a mother's response to both rewarding and stressful stimuli. Using functional magnetic resonance imaging in rodents, it was found that the activation of the dopaminergic reward system in response to nursing was attenuated when dams were exposed to cocaine before pregnancy (58). This study highlights the impact substances may have on the rewarding properties of maternal behavior. Additionally, rats exposed to cocaine postpartum show more aggressive behavior, but non-protective behavior towards their pups in response to intruders (59). These dams show alterations in their behavior toward stressful stimuli that negatively impact the care of their pups. In human mothers, a recent study by Landi and colleagues (60), using functional magnetic resonance imaging showed that substance using mothers had less activation in the PFC and limbic regions when compared non-using mothers in response to both infant faces and cries. This study provides evidence for a differential response to infant cues in substance using mothers in areas associated with motivation and reward, which may be due to dysregulation in the reward and stress neural pathways.

Thus, substance using mothers appear to display a differential sensitivity to rewarding and stressful stimuli. In the initial study, Rutherford et al. (6) explored whether this effect was manifested as a differential sensitivity to infant cues by investigating the processing of infant faces using electroencephalography (EEG). Two specific event-related potentials (ERP) were examined with regard to face processing: (1) N170, an early marker of the encoding of face structure, and (2) P1, an early marker of general visual processing. It was found that substance use modulated the latency of the N170, but not the P1, suggesting that this finding was specific to face processing and not a general slowing due to substance use.

In the current study, self-report measures completed by these mothers were analyzed to look for predictors of this differential neural response. It was hypothesized that substance-using mothers would score higher in measures of behavioral activation motivation system, impulsivity, and stress and lower in measures of behavioral inhibition motivation system relative to non-using mothers, given the underlying dysregulation of the reward and stress neural circuitry in addictive processes. Furthermore, it was hypothesized that these scores would correlate with a later latency of the N170, as the reward salience of the substance is greater than that of the infant cues in these substance using mothers, leading to decreased motivation towards the processing of infant faces.

Statement of Purpose

Specific Aims

- To further elucidate the relationship between addictive processes on the neural correlates of parenting, including maternal sensitivity to visual and auditory infant cues.
- To determine the predictors of the differential neural response to visual infant cues in substance using and non-using mothers.

Specific Hypotheses

- Substance using mothers will score higher in self-reported measures of the behavioral activation motivation system, impulsivity, and parental stress, and will score lower in the measure of the behavioral inhibition motivation system when compared to non-substance using mothers.
- The latency of the N170 peak will positively correlate with scores of the behavioral activation motivation system, impulsivity, and parental stress and inversely correlate with scores of the behavioral inhibition motivation system.

Methods

Participants

A total of 79 mothers were recruited from the New Haven community through drug treatment and rehabilitation centers, postpartum maternity wards, and flyers posted throughout the community. Informed consent was obtained from

all participants. The present study was part of a larger study that aimed to investigate the effect of substance use on the neural correlates of parenting.

In order to determine substance use status, a combination of self-report data and urine toxicology were collected at the intake approximately three months post-partum. Mothers were classified as substance using if they used any drugs or alcohol regularly during pregnancy or the postpartum period (n=22). Substances used by these mothers included tobacco, marijuana, heroin, amphetamines, methadone, alcohol, cocaine, opiates, or other substances not disclosed. More details of the determination of substance use status can be found in the manuscript by Landi et al (60). See Table 1 for complete breakdown of substances used.

The mean age in years of substance using mothers included in the final analysis was 26.82 (SD=5.66), while the mean age in years of non-substance using mothers was 29.37 (SD=6.74). Both had a mean number of children of 2, with a range of 1-6 children. Fifty-five percent (55%) of substance-using mothers and 38% of non-substance using mothers were African-American; and 23% and 46% respectively were Caucasian. The majority of substance using mothers reported that they were single (73%) followed by divorced (14%). The majority of non-substance using mothers were single (50%) followed by married (47%). There was a significant difference in marital status between substance using and non-using mothers ($\chi 2=11.48$, df=53, $p<.01$). There was also a significant difference in the mean years of education between groups, as non-substance using mothers had more years of education (15.48, SD=4.04) relative to non-using mothers (11.54, SD=2.00)

($t(45)=4.28$, $p<.001$). See Table 2 for complete breakdown of demographic information, including either a t-test or chi-square analysis for differences between substance using and non-using groups.

Apparatus and Stimuli

To measure EEG, a 128-electrode channel geodesic sensor net (Electrical Geodesics Incorporated) (61) was placed on the participant's head and fitted according to manufacture specifications, with electrodes spaced evenly and symmetrically across the scalp. EEG was recorded continuously at 250-Hz using NetStation 4.2.1 with high impedance amplifiers (0.1 Hz high pass, 100 Hz low pass). Electrodes were referenced to Cz during EEG recording. Impedances were kept below 40 kΩ. In order to investigate neural responses to both visual and auditory infant cues, both types of stimuli were presented to the mothers during the trials, as described below.

Visual stimuli. Visual stimuli were presented on a Pentium-IV computer controlling a 51 cm color monitor (75Hz, 1024 x 768 resolution) running E-Prime 1.2 software (62). Face stimuli were viewed at a distance of approximately 70 cm in a sound-attenuated room with low ambient illumination. Visual stimuli were comprised of photographs of infant faces between the ages of five and ten months adapted from previous work (63). A total of 126 images were used, with twenty-one different images from six infants. These images were balanced for gender and race (Caucasian and African-American) and were unfamiliar to the participants. The

infant faces were presented on a black background and measured, on average, 7.63° by 8.07° (9.32 cm by 9.88 cm). The infant faces displayed happy, neutral, and sad affect states, as rated by an independent group of 11 participants. In order to evaluate perceived affect level, face stimuli were rated on a scale of 1 (happy) to 10 (distressed). A repeated measures ANOVA of the infant face rating on the three emotions (happy, neutral, sad) was significant [$F(2, 20)=146.43$, $p<0.001$]. Pairwise comparisons showed that happy faces ($M=2.19$, $SE=0.24$) were rated as significantly less distressed (Mean difference=-1.55, $SE=0.37$, $p<0.01$) than neutral faces ($M=3.74$, $SE=0.43$), which were rated as significantly less distressed (Mean difference=-4.16, $SE=0.41$, $p<0.001$) than sad faces ($M=7.90$, $SE=0.11$).

Design

Trials consisted of centrally presented fixation cross, followed by the stimulus, and then a blank screen. Visual stimuli (infant faces) were presented for 300 ms and auditory stimuli (infant cries or neutral tone) were presented for 2000 ms. In order to avoid expectancy effects of stimulus onset, the inter-trial interval was varied during both the fixation cross and blank screen, ranging from 1400-2000 ms. Each participant underwent seven blocks of 42 trials, with each block containing 21 infant face presentations and 21 auditory presentations that were quasi-randomly presented, for a total of 252 experimental trials. The order of presentation was the same for each participant. There were 126 total visual stimuli trials, 42 trials for each of the happy, sad, and neutral conditions. There were 126 total

auditory stimuli trials, 42 trials for high distress, 44 trials for low distress, and 40 trials for the neutral tone.

In order to ensure that participants kept their attention to presentation of the stimuli, a one-back memory task was included throughout the course of the experiment. During these trials, a question mark replaced the fixation cross to indicate the impending memory task. Participants were asked to indicate whether the proceeding stimulus was the same or different to the next one presented, and communicated their response using a button box. These catch trials were not included in the analysis. There were an equal number of catch trials in which the stimulus was the same and different as the preceding one. These catch trials accounted for an additional 42 trials in the experiment for a grand total of 294 experimental and catch trials.

Prior to these trials, each participant underwent eight practice trials to familiarize herself with the procedure. Overall, the experiment was completed in approximately 30 minutes.

Self-Report Measures

After completing the EEG portion of the study, participants completed questionnaires to assess demographics and behavioral qualities. Participants completed the Barratt Impulsiveness Scale-11, the Behavioral Inhibition System/

Behavioral Activation System Scale, and the Parenting Stress Index-Short Form. Each questionnaire is described below.

Behavioral Inhibition System/Behavioral Activation System Scale (BIS/BAS) (65). The BIS/BAS scale is a 24-item self-report measure that is designed to assess the sensitivity of an individual's aversive and appetitive motivation systems. This scale is based on a theory proposed by Gray (22), who postulated that the aversive and appetitive motivation systems underlie two dimensions of personality: anxiety and impulsivity, respectively. The aversive motivation system, also known as the behavioral inhibition system, inhibits behavior that could lead to unpleasant or negative outcomes. The appetitive system, also known as the behavioral activation system, activates behavior that could lead to pleasant or rewarding outcomes. The scale measures three distinct but related components of the BAS, including drive, fun-seeking, and responsiveness to rewards. The drive subscale measures persistent pursuit of desired goals. The fun-seeking subscale measures a willingness to spontaneously approach an event that is potentially rewarding. The reward responsiveness subscale measures positive responses to the occurrence or anticipation of a reward.

All items are measured on a four-point Likert scale, where "1" represents "very true for me" and "4" represents "very false for me". All items except items 2 and 22 are scored in reverse. A score for the BIS and each component of the BAS is determined by the summation of the scores of specific items, and a higher score denotes a higher sensitivity with respect to that component.

Carver and White (65) report convergent and divergent validity of their scales with measures such as the Positive and Negative Affect Schedule, Minnesota Multiphasic Personality Inventory, and Eysenck and Eysenck's Extraversion scale. They also report adequate internal consistency, with Cronbach's alpha ranging from .66-.74.

Barratt Impulsiveness Scale-11 (BIS-11) (66). The BIS-11 is a 30-item self-report measure that is designed to assess the impulsivity of an individual. The scale is based on the idea that impulsivity is a multi-dimensional construct. Specifically, it assesses three second-order factors of impulsivity including attentional impulsiveness, motor impulsiveness, and non-planning impulsiveness, and six first-order factors of impulsivity including attention, motor, self-control, cognitive complexity, perseverance, and cognitive instability.

The items are measured on a four-point Likert scale, where "1" represents "Rarely/Never" and "4" represents "Almost Always/Always", with questions 1, 7, 8, 9, 10, 12, 13, 15, 20, 29, and 30 scored in the reverse. A score for each factor is determined by the summation of the scores of specific items, and a higher score denotes a more impulsive individual with respect to that factor.

Patton and colleagues (66) report high internal consistency of the BIS-11 among undergraduates, substance abuse patients, general psychiatric patients, and prison inmates, with Cronbach's alpha ranging from .79-.83. Additionally, the BIS-11 shows convergent validity among other self-report measures of impulsivity such as the Eysenck Impulsiveness Scale and Behavioral Measures of Impulsiveness (67).

Parenting Stress Index-Short Form (PSI-SF) (68). The PSI-SF is a 36-item self-report measure that is designed to assess stress in the relationship between parent and child. The index looks at parenting stress in three domains: parental distress, parent-child dysfunctional interaction, and difficult child. The parental distress score indicates the degree of personal stress such as conflict with a spouse that result from the limited ability to fulfill other roles when raising a child. The parent-child dysfunctional interaction score indicates the degree of stress from the interaction with the child. The difficult child score indicates the parent's perception of the child's inability to regulate his or her disruptive behavior. The PSI was designed to identify dysfunctional parenting and/or child behavior.

The items are measured on a five-point Likert scale, where "1" represents strongly agree and "5" represents "strongly disagree". A score for each domain is determined by the summation of the scores of 12 specific items, and a higher score denotes a higher level of stress in that domain.

The Parenting Stress Index and PSI-SF have been validated against measures including the Symptom Checklist-90-Revised and Brief Symptom Index, both measures of emotional health (68, 69). It has also been shown to have high reliability in both a largely Caucasian, married population (68) as well as a low-income, predominantly minority population (69).

Data Analysis

EEG Data

Pre-processing. The raw EEG data from each participant were pre-processed and prepared for statistical analysis using Net Station 4.2.1. For each experimental condition, data from each participant were averaged. A 30-Hz low-pass filter was applied to decrease environmental noise artifacts. Data were segmented from 100 ms before stimulus onset to 900 ms after stimulus onset. In order to control for eye blinks and movements, a threshold of 150 microvolts was implemented. Channels with artifacts in more than 50% of segments were marked as bad channels and replaced through spline interpolation (70). Segments that contained eye blinks, eye movement, and those with more than 20 bad channels were marked as bad and excluded from the analysis. On average 12 trials per participant were excluded. Participants with less than 25% remaining good trials were excluded (n=19), and six additional participants were excluded after excessive noise was noted on visual inspection, that had not been picked up by preprocessing protocols. The N170 was not discernible for these six participants. The final sample included 54 participants, comprised of 32 non-substance using mothers and 22 substance using mothers.

Statistical Analysis. For the analysis of face processing data, P1 and N170 ERPs were assessed at 12 electrodes: six electrodes over the left lateral posterior scalp (58, 59, 64, 65, 69, 70) and right lateral posterior scalp (90, 91, 94, 95, 96), as shown in Figure 1. These electrodes were selected based on the maximal observed N170 amplitude response to the infant faces. Furthermore, they correlate with the scalp

regions that characteristically elicit the N170 (42) and are the same electrodes that have been used to study the N170 in prior research using dense array EEG (48).

Using the Net Station user defined event function, time windows for the N170 and P1 were derived and customized for each participant. The function allows statistical extraction of each component to be representative of the variability in the waveforms. For the P1, the time window ranged across participants from 47 ms to 195 ms, and the P1 peak was defined as the maximum amplitude falling in that range. For the N170, the time window ranged across participants from 91 ms to 243 ms, and the N170 peak was defined as the minimum amplitude falling in that range.

P1 and N170 data were averaged from electrode sites within the left hemisphere and right hemisphere. Statistical analysis was conducted on amplitude and latency measures for each separate component (P1, N170) using repeated measures of analysis of variance (ANOVA). Specifically, the data were analyzed using a three (emotional expression: happy, neutral, sad) by two (hemisphere: left, right) within-subjects ANOVA with a between-group factor of substance using status (substance using, non-substance using). Effect size is presented as partial eta-squared ($\eta^2_{partial}$), where .01 represents small effect size, .06 represents a medium effect size, and .14 represents a large effect size, consistent with previous studies (49, 71). When applicable, Greenhouse-Geisser corrections were used.

Self-Report Measures

BIS/BAS Scale. Questionnaires from 53 participants were scored for five measures, including BIS sensitivity, BAS drive, BAS fun-seeking, BAS reward responsiveness, and BAS total, by adding the respective responses for each subset (65). .One mother was excluded for incomplete data. The mean score of each subset was determined for three groups: all participants (n=53), substance using mothers only (n=21), and non-substance using mothers only (n=32). The data for each of these three groups were further tested for normality using the Kolmogorov-Smirnov test.

BIS-11. Questionnaires from 54 participants were scored for nine measures, including the first-order factors (attentional impulsiveness, motor impulsiveness, and nonplanning impulsiveness) and second-order factors (attention, motor, self-control, cognitive complexity, perseverance, cognitive instability) of impulsiveness. The mean score of each subset was determined for three groups: all participants (n=54), substance using mothers only (n=22), and non-substance using mothers only (n=32). The data for each of these three groups were further tested for normality using the Kolmogorov-Smirnov test.

PSI-SF. Questionnaires from 45 participants were scored for three measures, including parental distress, parent-child dysfunctional interaction, and difficult child, by adding the respective responses for each subset. Nine mothers were excluded for incomplete data. The mean score of each subset was determined for three groups: all participants (n=45), substance using mothers only (n=21), and non-substance using mothers only (n=24). The data for each of these three groups were further tested for normality using the Kolmogorov-Smirnov test.

Statistical Analysis. For each self-report measure, the mean scores of each subset were examined for differences between substance using and non-substance using mothers. For groups in which the data for substance using and non-substance using mothers were both normally distributed, a t-test was used. For groups in which either one group or both were not normally distributed, the Mann-Whitney test was used. Statistical significance for differences between groups was determined using a Bonferroni-corrected alpha for multiple comparisons. For the BIS/BAS, significance was determined by an alpha of .05/5 or .01. For the BIS-11, significance was determined by an alpha of .05/9 or .0056. For the PSI-SF, significance was determined by an alpha of .05/3 or .012.

Given the apparent modulation of the N170 latency by substance use (see Results), correlations between the ERP components of visual stimuli and self-report measures were examined. Correlations between ERP components between auditory stimuli and self-report measures were not examined, as there appeared to be no significant modulation of the auditory ERP component (N100) by substance use. Specifically, there were no significant effects of substance use status on N100 amplitude [$F(1,52) = 1.10$, $p=.298$; $\eta^2_{partial}=.02$] and N100 latency [$F<1$; $\eta^2_{partial}=.01$].

The degree of correlation was determined between each of the visual ERP components (N170 latency, N170 amplitude, P1 latency, P1 amplitude) and the mean scores of each subset of BIS/BAS scale, BIS-11, and PSI-SF self-report measures for all mothers, substance using mothers only, and non-substance using mothers only. All ERP components were normally distributed. A Pearson correlation

coefficient (Pearson's r) was determined if the data from the subset were normally distributed. A Spearman's rho was determined if the data from the subset were not normally distributed. Statistical significance of each correlation coefficient was determined using a Bonferroni-corrected alpha for multiple comparisons. For the BIS/BAS, significance was determined by an alpha of .05/20 or .0025. For the BIS-11, significance was determined by an alpha of .05/36 or .0014. For the PSI-SF, significance was determined by an alpha of .05/12 or .0042.

Results

Catch Trial Response

Of the women included in the final analyses, overall accuracy was 91% for auditory stimuli and 95% for visual stimuli (n=48; four participants did not have accuracy data due to technical issues with E-prime response recording).

ERP Data for Infant Faces

P1 Amplitude. The P1 amplitude was not modulated by emotional expression [$F<1$; $\eta^2_{partial}<.01$], hemisphere [$F<1$; $\eta^2_{partial}=.01$], or substance use status [$F(1,52) = 1.32$, $p=.255$; $\eta^2_{partial}=.03$]. There was a marginal, non-significant interaction between emotional expression and substance use status [$F(2,104) = 2.73$, $p=.070$; $\eta^2_{partial}=.05$], and there were no other significant interactions [$F's<1$; $\eta^2_{partial}\leq.01$]. There

were no effects of emotion, hemisphere, or their interactions in substance using or non-substance using mothers separately.

P1 Latency. The P1 latency was not modulated by emotional expression [$F<1$; $\eta^2_{partial}<.01$], hemisphere [$F(1,52) = 1.30$, $p=.259$; $\eta^2_{partial}=.02$], or substance use status [$F(1,52) = 1.19$, $p=.28$; $\eta^2_{partial}=.02$]. There were no other significant interactions between these variables [$F's<1.77$; $p's>.175$; $\eta^2_{partial}<.03$].

Thus, these findings suggest that the P1 as a marker of early perceptual processing of visual stimuli was unaffected by infant emotional expression and substance use status of the mothers in this sample.

N170 Amplitude. The N170 amplitude was not modulated by emotional expression [$F<1$; $\eta^2_{partial}=.01$], hemisphere [$F<1$; $\eta^2_{partial}=.02$], substance use status [$F(1,52) = 1.60$, $p=.211$; $\eta^2_{partial}=.03$]. There were no other significant interactions between these variables [all $F's<1.48$; $p's>.234$; $\eta^2_{partial}<.03$].

N170 Latency. There was a significant modulation of the N170 latency by substance use status [$F(1,52)=6.08$, $p=.017$; $\eta^2_{partial}=.11$]. Compared to non-substance using mothers, the N170 latency in substance using mothers was later (Mean N170 latency = 168.05 ± 17.96 ms versus 158.00 ± 12.01 ms, $p=.017$). The N170 latency was unaffected by emotion [$F(2,104)=1.81$, $p=.168$; $\eta^2_{partial}=.03$] and hemisphere [$F(1,52)=1.62$, $p=.208$; $\eta^2_{partial}=.03$]. There were no other significant interactions between these variables [all $F's<1$; $\eta^2_{partial}<.01$].

Thus, these findings suggest that the N170 as a marker of early structural encoding on infant faces is modulated by maternal substance use.

Self-Report Measures and Correlations with ERP Data

BIS/BAS scale. As presented in Table 3, substance using mothers had higher mean scores in the BAS subscales and a lower mean score in the BIS scale compared to non-substance using mothers, although these differences were not statistically significant. Substance using mothers scored slightly higher than non-using mothers on the BAS fun-seeking element, though this difference was also not statistically significant (Mean score = 11.83 ± 2.17 versus 11.13 ± 2.20, Mann-Whitney U= 253, n_1= 31, n_2= 22, p=.11).

As can be seen in Figure 2, there was a small correlation between the N170 latency and BAS fun-seeking score in all mothers (Pearson's r = .274, p<.05). No correlation was observed in substance using mothers alone (Spearman's rho = .093, p=.68) and a medium correlation was observed in non-substance using mothers alone (Pearson's r = .355, p=.05). In addition, there was a small correlation between the P1 latency and the BAS fun-seeking score in all mothers (Pearson's r = .256, p=.07). Table 4 summarizes the results between all ERP components and the BIS/BAS subscales in all mothers.

Taken together, these findings suggest that substance using mothers have higher BAS sensitivity and lower BIS sensitivity, though these findings were not

statistically significant, and that across the entire sample of women, a larger N170 latency is associated with a higher BAS fun-seeking score.

BIS-11. Substance using mothers had higher mean scores in all nine measures of impulsivity compared to non-substance using mothers, as shown in Table 5. Substance using mothers scored significantly higher than non-using mothers in the motor impulsiveness factor of impulsivity.

As shown in Figure 3, there was a small correlation between the cognitive complexity factor and N170 latency (Pearson's r = .260, p=.06), where later latency is associated with higher cognitive complexity scores. This correlation was not observed in substance using mothers alone (Spearman's rho = .175, p=.44) or non-using mothers alone (Spearman's rho = .080, p=.66). There was no correlation between the cognitive complexity factor and P1 latency (Pearson's r = .049, p=.73). Table 6 summarizes the results between all ERP components and the BIS-11 subscales in all mothers.

Thus, these findings suggest that substance using mothers score higher on measures of impulsivity and that across the entire sample of women, a larger N170 latency is associated with a higher level of impulsivity related to cognitive complexity.

PSI-SF. No significant differences were found in measures of parenting stress between substance using mothers relative to non-using mothers, as shown in Table 7. Substance using mothers had higher mean scores, though statistically non-

significant, in parental distress compared to non-substance using mothers (Mean score = 25.57 ± 9.87 versus 23.37 ± 7.11, t(52)= -0.864, p=.39).

As shown in Figure 4, there was a small correlation between parental distress and N170 latency (Pearson's r = .253, p=.09), where later latency is associated with higher parental distress scores. There was a medium correlation between parental distress and N170 latency in substance using mothers alone (Pearson's r = .324, p=.15), though no correlation existed in non-using mothers alone (Pearson's r = .045, p=.84). There was a smaller correlation between parental distress and P1 latency (Pearson's r = .148, p=.33). Table 8 summarizes the results between ERP components and PSI-SF subscales in all mothers.

Thus, these findings suggest that substance using mothers have a higher level of parental distress, though this finding was not statistically significant, and that across the entire sample of women, a larger N170 latency is associated with a higher level of parental distress.

Discussion

In the present study, self-report measures of motivation, impulsivity, and stress were analyzed to identify potential predictors of a differential neural response to visual infant cues in substance using and non-using mothers. In the initial study, it was found that the face-specific N170 ERP component peaked later in substance using mothers when compared to non-using mothers. This modulation of

the N170 by substance use was not seen in the P1, an early marker of visual processing, suggesting that the finding did not reflect a generalized slowing of perceptual processes related to substance use. In the current study, we found that the later latency of the N170 peak was predicted by higher sensitivity to fun-seeking behavioral motivation, higher levels of the cognitive complexity factor of impulsivity, and higher levels of parental distress. These results provide further insight into the behavioral manifestations of differential early perceptual processing of infant faces.

Behavioral Motivation Systems

We found that substance using mothers relative to non-using mothers had a higher sensitivity to all BAS components and a lower sensitivity to BIS, although the differences were not statistically significant when controlled for multiple comparisons. In a study utilizing the BIS/BAS scales in college students, drug addicted individuals were found to have significantly higher BAS fun-seeking, drive, and total scores when compared to healthy controls (78). Thus, the absence of significant differences in BIS/BAS sensitivity between the groups of the present study may be a result of a more moderate severity of drug use among the sample of mothers relative to the drug addicted sample. The severity of drug use was not measured in this sample of mothers, an important limitation to this study (discussed below). In addition, the absence of significance differences may also be related to the sample size.

We found a small correlation between N170 latency and BAS fun-seeking score in all mothers, though this did not reach statistical significance after controlling for multiple comparisons. Specifically, a later N170 latency was associated with a higher BAS fun-seeking score. This correlation appeared to be driven primarily by the non-substance using group. This effect may not have shown up in the substance using group due to its small sample size. Importantly, a higher BAS-fun seeking score was also associated with a later P1 latency. Thus, the effect may in fact represent a generalized slowing of visual processing and more investigation will be necessary before these results are generalized.

The N170 has previously been shown to be modulated by the motivational significance of a stimulus (79). In this study, the N170 amplitude was smaller in response to faces associated with monetary reward relative to unrewarded faces, suggesting a preferential processing and a more efficient structural encoding process for faces associated with reward. In contrast to the present study, the results showed no effect of motivation on N170 latency. The correlation between the N170 and BAS fun-seeking found in the present study may in fact represent delayed engagement to the stimulus as influenced by its reward salience. The fun-seeking component measures a willingness to spontaneously approach a novel event (80). This type of behavior is expected in drug-seeking individuals, as they are strongly motivated to acquire substances and are willing to approach novel situations in order to achieve this goal. It has been proposed that the fun-seeking component of the BAS is related to both reward reactivity and impulsivity (81) both of which appear to be altered in addictive processes (5, 82). This alteration in the

behavioral activation system with substances serving as the primary motivation may then lead to delayed engagement of rewarding non-substance stimuli, such as infant cues, which was manifested as a delayed latency of the N170 peak in response to infant faces in the present study.

Impulsivity

Substance using mothers scored significantly higher on the second-order impulsivity factor of motor impulsiveness. They also scored higher on all other measures of impulsivity, including the cognitive complexity factor, though these results did not reach statistical significance after controlling for multiple comparisons. These results are consistent with previous findings, as substance use has been associated with higher levels of impulsivity on both self-report and neurocognitive measures (82). Although impulsivity has been examined extensively in relation to psychostimulants, it has also been linked to opiates, alcohol, MDMA, and nicotine use.

We found a small correlation between cognitive complexity factor of impulsivity and N170 latency across the entire sample of women, though this did not reach statistical significance after controlling for multiple comparisons. Specifically, a later N170 latency was associated with a higher score of the cognitive complexity factor of impulsivity. Patton and colleagues (66) describe the cognitive complexity factor as the degree to which an individual "enjoy[s] challenging mental tasks", with a higher score denoting less pleasure derived from these mental tasks.

Given this deficit in cognitive complexity, an impulsive mother may not find the same reward salience in her infant's cues, or be able to compute the reward value related to her infant. For instance, excessive crying and colic are commonly reported behaviors in early infancy to which a mother must respond (83). Crying syndromes can represent a response to a distinct organic cause in <5% of cases or normal crying behavior (84), and consoling a crying infant requires complex thinking by the mother in order to determine the source of the infant's distress. Difficult infant temperament is associated with maternal anxiety (85), and complex thought process is necessary for the mother to realize that responding to the cry is associated with a delayed reward. Thus, if a mother did not enjoy complex thinking, she would not find caring for her infant as rewarding. In the present study, this decreased reward salience to infant cues may have been manifested as a differential early perceptual processing of infant faces. Furthermore, the cognitive complexity factor of impulsivity is expected in addictive behaviors, as individuals may be less likely to think about the future consequences of their actions, acting with the drug as their primary motivation at the cost of their infant's well-being.

Stress

Surprisingly, no statistically significant differences were found in measures of parenting stress in substance using mothers relative to non-using mothers. It was hypothesized substance using mothers would perceive infant cues as more stressful, and they would therefore score higher on the difficult child subscale compared to

non-using mothers. Furthermore, it was hypothesized that their interactions with the infant would have less reward salience relative to non-using mothers, and they would therefore score higher on the parent-child dysfunctional interaction subscale. However, these findings were not observed in our study. It was found that substance using mothers scored higher on the Parental Distress subscale, though this finding was not statistically significant.

An important limitation to the study of self-report measures of parenting stress is response bias, or reporting answers that the participant presumes to be more socially desirable (86). In one study, reporting everyday hassles was negatively associated with social desirability; the authors of this study suggest this is because reporting everyday hassles indicates an inability to handle daily life, which may be frowned upon by others (87). Similarly, mothers in the present study may be less likely to report the stress associated with parenting as it may not be viewed favorably, which may have affected our ability to pick up significant differences between the substance using and non-using groups. Another important limitation to the analysis of the PSI-SF self-report measures was the smaller sample size (n=45). Nine women were excluded due to incomplete data, which may have affected the ability of the analysis to pick up significant differences between groups, and perhaps additional significant correlations between measures of parental stress and the N170.

We found a small correlation between parental distress and N170 latency, though this did not reach statistical significance after controlling for multiple

comparisons. Specifically, a later N170 latency was associated with a higher parental distress score. This effect appeared to be driven primarily by the substance using group. The parental distress score indicates distress associated with personal factors such as conflict with a spouse that result from the limited ability the parent has to fulfill other roles due to the demands of raising a child (69). This correlation may represent a consequence of the interaction between altered reward and stress pathways in addictive processes. Oxytocin may play a role in downregulating stress in human mothers, as suggested by a recent study in which interactions with infants activated reward pathways and increased peripheral oxytocin (8), which is thought to mediate a hyporesponsive reaction to stress in the peripartum period (29). Within this context, the correlation between the N170 latency and parental distress may in fact represent heightened stress reactivity as a result of the attenuation of the rewarding value of infant cues in substance using mothers.

Limitations and Considerations

The results of this study must be considered in light of its limitations. The discussion highlights trends noted among the sample, which we would be cautious about generalizing without further investigation. Importantly, the absence of statistically significant correlations between ERP components and the self-report measures does not discount the importance of these trends. One limitation that may account for this includes the small sample size, which may have affected the power of the study to pick up significant differences.

The present study was based under the framework that substance use as a whole represents an addictive process, motivated by the reward of drug use and relief of negative affect associated with withdrawal. However, one important limitation of this study is that a differentiation between severities of substance use among women in this sample was not made. The magnitude of the effect of substances on the reward and stress pathways likely depends on the severity of substance use, with a greater degree of dysregulation occurring in individuals who are dependent on these drugs. DSM-IV criteria of substance dependence include tolerance and withdrawal, two extreme manifestations of the dysregulation of the stress and reward neural circuitry, which are not necessarily seen in substance abuse or substance use (88). It is possible that the women in this sample represent substance users of moderate severity, in whom the degree of dysregulation was not substantial enough to allow for significant differences in behavioral measures or their correlations with the ERP components. A related limitation is that the substances used by the women in the sample were varied, and further investigation in more homogenous samples is warranted before these results are generalized.

As mentioned previously, an important limitation of self-report measures of attitudes and behaviors in empirical research is the response bias (86). In the present study, the participant may have viewed unregulated motivation, higher impulsivity, and enhanced stress reactivity as socially undesirable and thus reported these responses less, which may have limited our ability to pick up significant differences between substance using and non-using groups. Future investigation could supplement the present study by looking at laboratory measures

of impulsivity, such the Stroop test and delay discounting tasks (82). In addition, investigation involving physiological markers of stress, such as changes in cortisol levels (89) or heart rate (90), could serve to validate our self-report measures of stress. Additionally, substance using mothers differed significantly from non-using mothers with respect to their years of education. Differences in literacy or perhaps even impaired cognition due to substance use may have influenced their ability to complete the self-report measures properly, which may also have influenced our results. This highlights the importance of utilizing more objective techniques, such as the EEG, in investigating differences between substance using mothers and non-using mothers.

Finally, future research should investigate later, more cognitive components of the ERP waveform in substance using and non-using mothers. The present study focused on early perceptual components of the ERP, looking at rapid responses to infant cues. This notion is consistent with the theory of intuitive parenting proposed by Papousek and Papousek (91), or the notion that parenting can include behaviors of which the parent is not consciously aware. An ERP component that may be of interest is the late positive potential (LPP), which has been implicated as a marker of emotional processing (92). Interestingly, it has been implicated in the reappraisal of emotionally evocative stimuli in response to internal and external factors (93). Substance use may serve as an external factor that alters a mother's perceived salience of emotionally evocative infant stimuli, which may in turn impair her ability to respond to these cues. The design of the present study can be applied to future investigation involving the LPP.

Conclusion

In summary, the present study investigated predictors of a differential neural response to visual infant cues in substance using and non-using mothers. We found that substance using mothers scored higher on BAS fun-seeking sensitivity, the cognitive complexity factor of impulsivity, and parental distress. Furthermore, we found that across the entire sample of mothers, the later latency of the N170 was predicted by a higher sensitivity to the fun-seeking component of the BAS and higher levels of both the cognitive complexity factor of impulsivity and parental distress. We interpret these findings to suggest that early visual processing of infant faces may be compromised in mothers with higher sensitivity to the fun-seeking component of the BAS, higher levels of impulsivity related to cognitive complexity, and higher levels of parental distress, as all lead to reduced salience of rewarding infant cues. Because these traits were more likely to be found in substance using mothers, these results lend further support to the hypothesis that dysregulation of the reward and stress pathways occur in addictive processes, which may in turn affect parenting by altering sensitivity to infant cues.

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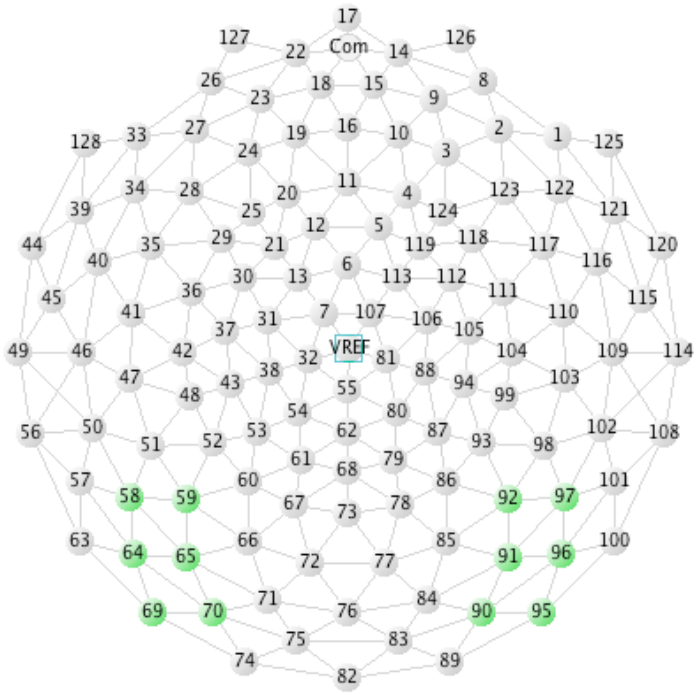

Figure 1. Electrode layout for geodesic sensor net (Electrical Geodesics Incorporated) (61) . P1 and N170 ERPs were determined by averaging latency at 6 electrodes over left (58, 59, 64, 65, 69, 70) and right (90, 91, 92, 95, 96, 97) scalp sites.

Table 1. Substances used by mothers (n=31; 1 participant in rehabilitation treatment)

Substance	Percentage reporting use
Tobacco	71%
Marijuana	19%
Heroin	3%
Amphetamines	3%
Methadone	3%
Alcohol	6%
Cocaine	6%
Opiates	3%
Other substance not disclosed	19%

Table 2. Demographic and parenting information for mothers included in the final analyses. For ethnicity and marital status, absolute numbers and group percentage (presented in parentheses) are reported. t or χ2 statistic presented to compare differences between substance using and non-using mothers.

	Non-substance using mothers (n=32)	**Substance using mothers (n=22)**	**t or χ2**	***p***
Mean Age (years)	29.37 (SD=6.74)	26.82 (SD=5.66)	1.459	0.15
Mean Number of Children	2 (range 1-6 children)[a]	2 (range 1-6 children)[b]	-1.444	0.16
Mean Years of Education	15.48 (SD=4.04)[c]	11.54 (SD=2.00)[b]	4.28	<0.001*
Ethnicity			6.964‡	0.32
African-American	12 (38%)	12 (55%)		
Asian-American	1 (3%)	0 (0%)		
Caucasian	15 (46%)	5 (23%)		
Caucasian/African-American	1 (3%)	0 (0%)		
Hispanic	1 (3%)	2 (9%)		
Hispanic/Latino	2 (6%)	3 (14%)		
Marital Status			11.48‡	0.01*
Single	16 (50%)	16 (73%)		
Married	15 (47%)	2 (9%)		
Divorced	0 (0%)	3 (14%)		
Widowed	0 (0%)	0 (0%)		
Not reported	1 (3%)	1 (5%)		

*p<.05

‡ χ2 was calculated to determine differences between substance using and non-using groups. If not denoted as such, the statistic calculated is a t-statistic.

a- 3 mothers did not report
b- 1 mother did not report
c- 7 mothers did not report

SD = standard deviation

Table 3. Mean scores on BIS/BAS scale, presented as the mean score ± SD. t or U statistic presented compares substance using mothers and non-using mothers.

	Total (n=53)	Substance Using Mothers (n=22)	Non-substance using mothers (n=31)	t or U statistic	*p*
BAS Drive	11.28 ± 2.74	12.09 ± 2.22	10.70 ± 2.95	-1.86	0.07
BAS Fun-seeking	11.42 ± 2.20	11.83 ± 2.17	11.13 ± 2.20	253‡	0.11
BAS Reward Responsiveness	17.33 ± 2.08	17.76 ± 2.02	17.03 ± 2.11	271‡	0.20
BAS Total	40.03 ± 6.03	41.69 ± 5.44	38.86 ± 6.24	250‡	0.10
BIS	19.48 ± 3.78	19.42 ± 3.13	19.52 ± 4.23	0.086	0.93

‡ Mann-Whitney U statistic was calculated to determine differences between substance using and non-using groups. If not denoted as such, the statistic calculated is a t-statistic.

Table 4. Correlations between BIS/BAS scale and ERP components in all mothers.

		N170 latency	N170 amplitude	P1 latency	P1 amplitude
BAS Drive	Correlation coefficient	0.191	-0.04	0.096	-0.156
	Sig. (2-tailed)	0.17	0.78	0.49	0.27
BAS Fun-seeking	Correlation coefficient	0.274*	0.061	0.256	-0.112
	Sig. (2-tailed)	<.05	0.67	0.07	0.43
BAS Reward Responsiveness	Correlation coefficient‡	0.112	-0.288*	-0.133	-0.309*
	Sig. (2-tailed)	0.43	0.04	0.34	0.03
BAS Total	Correlation coefficient	0.218	-0.111	0.098	-0.225
	Sig. (2-tailed)	0.12	0.43	0.49	0.11
BIS	Correlation coefficient	0.044	0.058	-0.015	-0.176
	Sig. (2-tailed)	0.75	0.68	0.92	0.21

* $p < .05$

‡ Spearman's rho. Correlation coefficients that are not denoted as such represent Pearson's correlation coefficients.

Figure 2. Correlation between BAS fun-seeking score and N170 latency, Pearson's r = .274, p<.05.

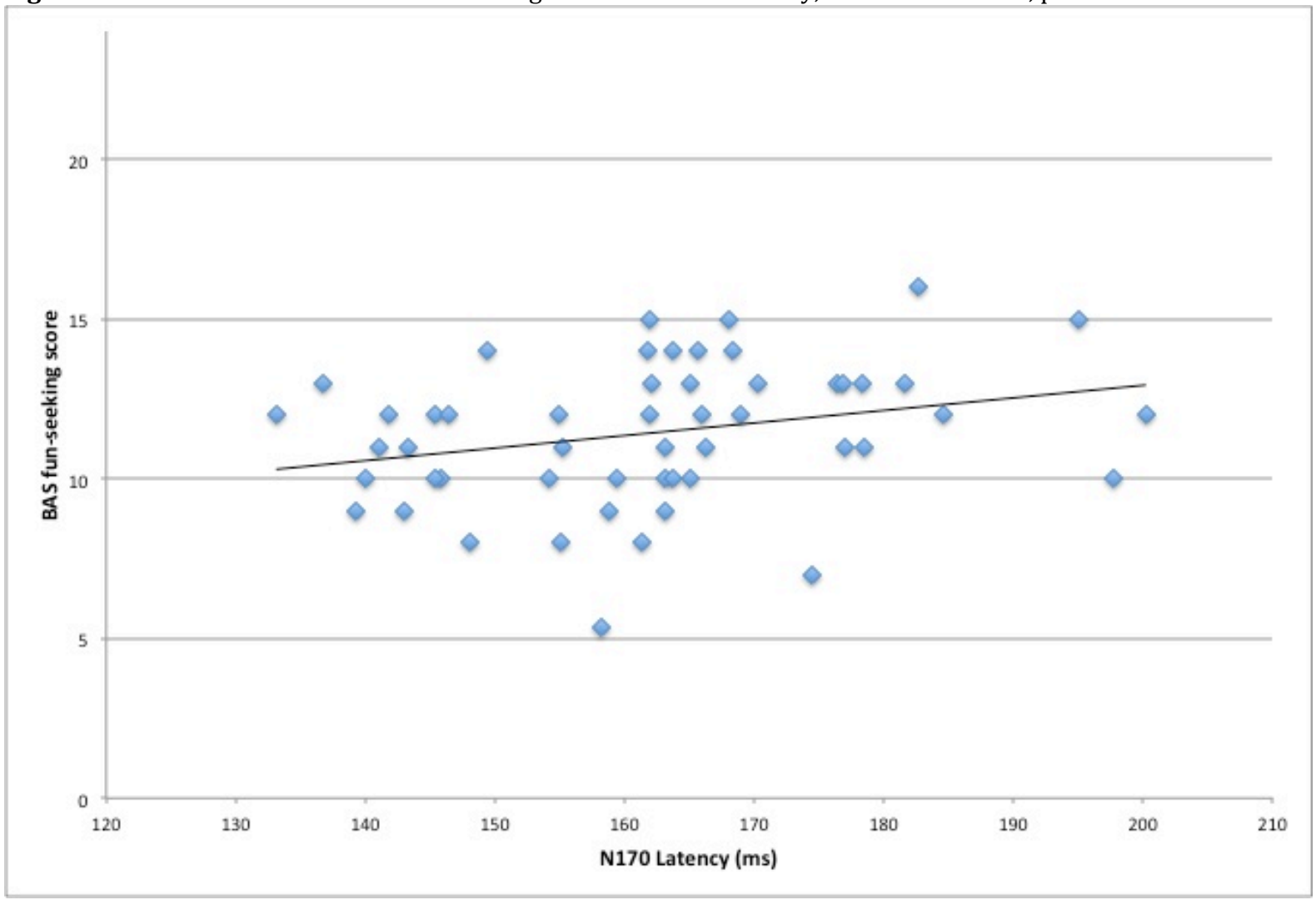

Table 5. Mean scores on BIS-11, presented as mean ± SD. t or U statistic presented compares substance using mothers and non-using mothers.

	Total (n=54)	Substance Using Mothers (n=22)	Non-substance using mothers (n=32)	U or t statistic	*p*
Attention	8.67 ± 2.66	8.86 ± 2.95	8.53 ± 2.46	340.50‡	0.84
Motor	14.02 ± 2.66	15.32 ± 2.40	13.13 ± 2.49	178.5‡	<.01*
Self-Control	11.02 ± 3.15	11.91 ± 3.31	10.41 ± 2.94	-1.75	0.085
Cognitive Complexity	10.56 ± 2.52	11.27 ± 2.49	10.06 ± 2.45	238.00‡	.04*
Perseverance	7.04 ± 1.97	7.82 ± 2.20	6.50 ± 1.63	217.50‡	.02*
Cognitive Instability	5.17 ± 1.58	5.36 ± 1.29	5.03 ± 1.75	-0.759	0.45
Attentional Impulsiveness	13.83 ± 3.42	14.23 ± 3.61	13.56 ± 3.32	322.00‡	0.596
Motor Impulsiveness	21.06 ± 3.67	23.14 ± 3.50	19.63 ± 3.09	143.5‡	<.001***
Nonplanning Impulsiveness	21.57 ± 4.91	23.18 ± 5.31	20.47 ± 4.36	-2.06	<.05*

* $p < .05$

*** $p < .0056$ (Bonferroni-corrected significance level)

‡ Mann-Whitney U statistic was calculated to determine differences between substance using and non-using groups. If not denoted as such, the statistic calculated is a t-statistic.

Table 6. Correlations between BIS-11 subscales and ERP components in all mothers (n=54).

		N170 latency	N170 amplitude	P1 latency	P1 amplitude
Attention	Correlation coefficient‡	0.068	0.034	0.108	0.185
	Sig. (2-tailed)	0.82	0.81	0.44	0.18
Motor	Correlation coefficient‡	0.031	-0.039	0.036	-0.09
	Sig. (2-tailed)	0.82	0.78	0.79	0.52
Self-Control	Correlation coefficient	0.023	0.103	-0.028	0.11
	Sig. (2-tailed)	0.87	0.46	0.84	0.43
Cognitive Complexity	Correlation coefficient	0.26	0.058	0.148	0.049
	Sig. (2-tailed)	0.06	0.68	0.28	0.73
Perseverance	Correlation coefficient‡	0.226	0.026	0.128	0.197
	Sig. (2-tailed)	0.10	0.85	0.35	0.15
Cognitive Instability	Correlation coefficient‡	0.187	0.199	.319*	0.253
	Sig. (2-tailed)	0.18	0.150	0.02	0.07
Attentional Impulsiveness	Correlation coefficient	0.16	0.145	0.201	.276*
	Sig. (2-tailed)	0.25	0.30	0.15	0.04
Motor Impulsiveness	Correlation coefficient‡	0.177	-0.012	0.129	0.018
	Sig. (2-tailed)	0.20	0.93	0.35	0.90
Nonplanning Impulsiveness	Correlation coefficient	0.148	0.096	0.058	0.096
	Sig. (2-tailed)	0.29	0.49	0.68	0.49

* $p < .05$

‡ Spearman's rho. Correlation coefficients that are not denoted as such represent Pearson's correlation coefficients.

Figure 3. Correlation between Cognitive Complexity and N170 Latency, Pearson's r = .06

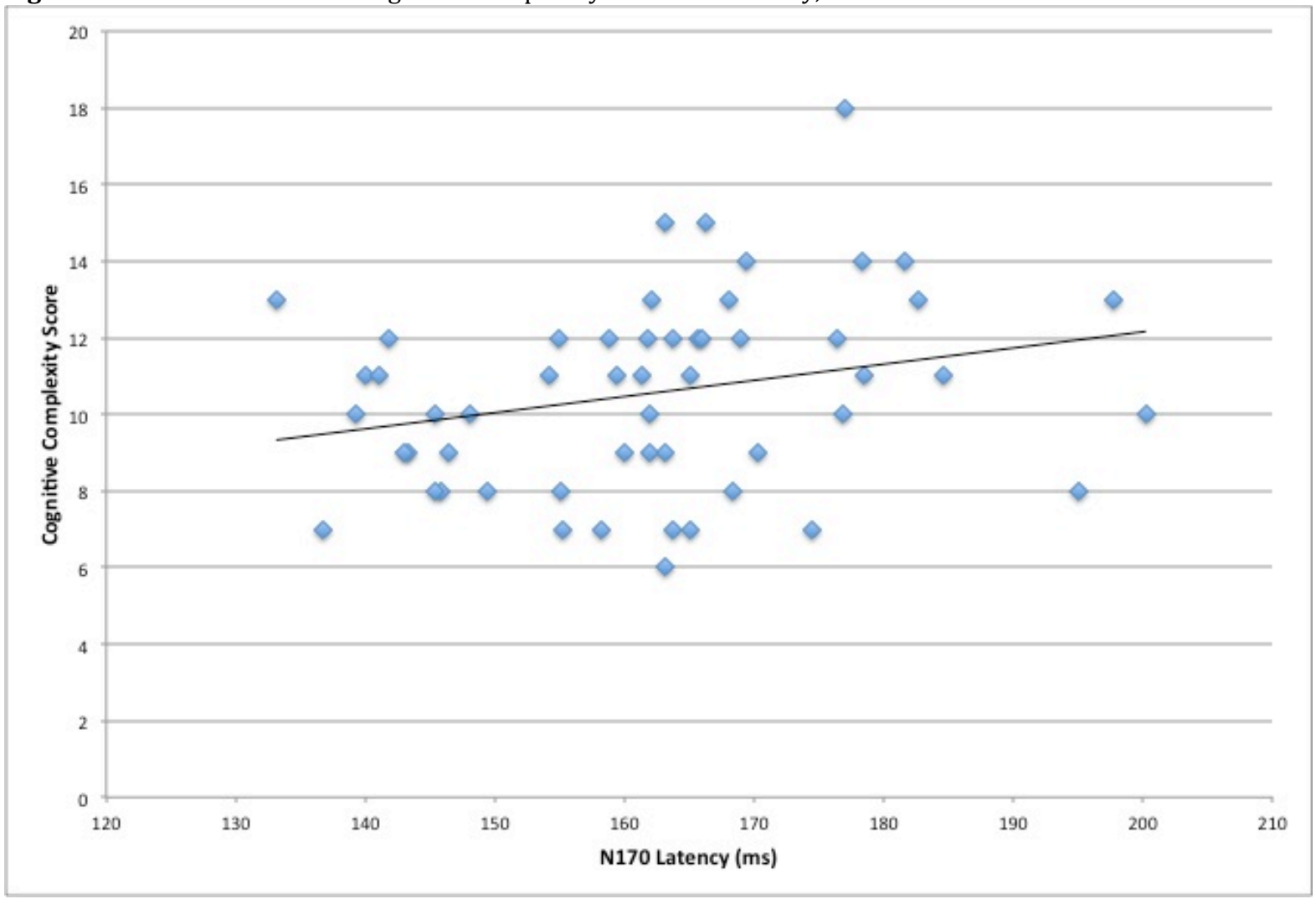

Table 7. Mean scores on PSI-SF, presented as mean ± SD. t or U statistic presented compares substance using mothers and non-using mothers.

	Total (n=53)	Substance Using Mothers (n=22)	Non-substance using mothers (n=24)	U or t statistic	*p*
Parental Distress	24.40 ± 8.48	25.57 ± 9.87	23.37 ± 7.11	-0.864	0.39
Parent-Child Dysfunctional Interaction	17.14 ± 6.00	16.68 ± 5.23	17.62 ± 6.76	227.00‡	0.92
Difficult Child	20.85 ± 6.96	20.00 ± 6.99	21.75 ± 7.00	171.00‡	0.31

‡ Mann-Whitney U statistic was calculated to determine differences between substance using and non-using groups. If not denoted as such, the statistic calculated is a t-statistic.

Table 8. Correlations between PSI-SF subscales and ERP components in all mothers.

		N170 Amplitude	N170 Latency	P1 Amplitude	P1 Latency
Parental Distress	Correlation Coefficient	0.221	0.253	0.066	0.148
	Sig. (2-tailed)	0.14	0.09	0.67	0.33
Parent-Child Dysfunctional Interaction	Correlation Coefficient‡	0.172	0.131	0.084	0.223
	Sig. (2-tailed)	0.27	0.40	0.59	0.15
Difficult Child	Correlation Coefficient‡	0.049	0.138	-0.027	0.049
	Sig. (2-tailed)	0.76	0.39	0.87	0.76

‡ Spearman's rho. Correlation coefficients that are not denoted as such represent Pearson's correlation coefficients.

Figure 4. Correlation between Parental Distress and N170 Latency, Pearson's r = .253, p=.09.